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CYTYC CORPORATION
Darry Pattinson, Sr. IP Paralegal
250 CAMPUS DRIVE
MARLBOROUGH, MA 01752

EXAMINER	
MUMMERT, STEPHANIE KANE	
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte JAMES LINDER, MICHAEL COHENFORD, ERIN COFFMAN and BRIAN B. LENTRICHIA

Appeal 2008-2363
Application 10/618,443
Technology Center 1600

Decided:[1] March 30, 2009

Before TONI R. SCHEINER, DEMETRA J. MILLS, and ERIC GRIMES, *Administrative Patent Judges*.

SCHEINER, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the rejection of claims 1-23, 26-29, 36, and 37, all the claims pending. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, begins to run from the decided date shown on this page of the decision. The time period does not run from the Mail Date (paper delivery) or Notification Date (electronic delivery).

STATEMENT OF THE CASE

"This invention relates to methods . . . useful in detecting target substances in an alcoholic preservative solution, and for identifying sensors useful for binding to such targets" (Spec. 1: 8-10). Independent claims 1 and 28 are representative of the subject matter on appeal:

1. An assay method comprising:
providing a sample that is suspected of containing a target;
providing a sensor that can bind to the target in an alcoholic preservative solution that does not contain formamide, said sensor conjugated to a chromophore;
contacting the sample with the sensor in the alcoholic preservative solution that does not contain formamide under conditions in which the sensor can bind to the target, if present;
applying a light source to the solution that can excite the chromophore; and
detecting whether light is emitted from the target.

28. A method for identifying a sensor which specifically binds to a desired target, comprising:
contacting a sample suspected of containing a target of interest with a detectable sensor,
wherein said contacting takes place in a preservative solution comprising an amount of one or more water-soluble alcohols effective to preserve such solution against at least one contaminant and does not contain formamide, and detecting whether said sensor has bound to said target.

The Examiner relies on the following evidence:

Ylikoski et al.	US 5,256,535	Oct. 26, 1993
Shah et al.	US 6,165,723	Dec. 26, 2000
Hyldig-Nielsen et al.	US 6,280,946 B2	Aug. 28, 2001
Lorincz et al.	US 6,969,585 B2	Nov. 29, 2005
Challberg et al.	WO 93/10263	May 27, 1993

Kenji Fukasawa et al., *Abnormal Centrosome Amplification in the Absence of p53*, 271 SCIENCE 1744-1747 (1996).

Marcel Bruchez Jr., et al., *Semiconductor Nanocrystals as Fluorescent Biological Labels*, 281 SCIENCE 2013-2016 (1998).

Ravindra Kumar et al., *The First Analogues of LNA (Locked Nucleic Acids): Phosphorothioate-LNA and 2'-Thio-LNA*, 8 BIOORGANIC & MEDICINAL CHEMISTRY 2219-2222 (1998).

The claims stand rejected as follows:

- Claim 28 under 35 U.S.C. § 102(e) as anticipated by Lorincz.
- Claims 1-4, 8-12, 14-16, 18, 19, 23, 26, and 27 under 35 U.S.C. § 103(a) as unpatentable over Lorincz and Shah.[2]
- Claims 20-22 under 35 U.S.C. § 103(a) as unpatentable over Lorincz, Shah, and Challberg.
- Claim 29 under 35 U.S.C. § 103(a) as unpatentable over Lorincz and Challberg.
- Claims 5, 7, 29, 36, and 37 under 35 U.S.C. § 103(a) as unpatentable over Lorincz, Shah, and Hyldig-Nielsen.
- Claim 6 under 35 U.S.C. § 103(a) as unpatentable over Lorincz, Shah, and Kumar.
- Claim 10 under 35 U.S.C. § 103(a) as unpatentable over Lorincz, Shah, and Bruchez.
- Claim 13 under 35 U.S.C. § 103(a) as unpatentable over Lorincz, Shah, and Ylikoski.
- Claim 17 under 35 U.S.C. § 103(a) as unpatentable over Lorincz, Shah, and Fukasawa.

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[2] Both the Examiner and Appellants list claims 24 and 25 in this rejection, but claims 24 and 25 have been canceled (App. Br. 2).

ISSUE: ANTICIPATION

The issue raised by this rejection on appeal is whether Appellants have established that the Examiner erred in finding that Lorincz describes contacting a sample suspected of containing a target of interest with a detectable sensor, where contacting takes place in a water-soluble alcohol-containing preservative solution.

FINDINGS OF FACT

FF1 The Examiner rejected claim 28 as anticipated by Lorincz. Claim 28 is directed to a method for identifying a sensor which specifically binds to a desired target. The method comprises contacting a sample suspected of containing the target with a detectable sensor, "wherein said contacting takes place in a preservative solution" comprising one or more water-soluble alcohols in an amount effective to preserve the solution against at least one (unspecified) contaminant (for an unspecified period of time), and wherein the preservative solution does not contain formamide, and detecting whether the sensor has bound to the target.

FF2 The Specification teaches that "the preservative solution comprises a water-miscible alcohol . . . present in an amount sufficient to fix sample cells or tissue while still permitting acceptable binding of the sensor to its target. The alcohol . . . may be selected from the group consisting of methanol, ethanol and isopropanol" (Spec. 22: 11-16).

> In one embodiment of the invention, the alcohol is present at a level sufficient for fixing and preserving the sample component of interest, and may be present in an amount greater than about 40% and less than about 60% . . . if the concentration of alcohol in this embodiment is at 40% or below, the cells are not sufficiently fixed for relatively long-term preservation . . . .

> In another embodiment of the invention, the alcohol is present in an amount of at least approximately 20 percent by solution. While this concentration of alcohol, as noted above, does not enable long term preservation, (i.e., over two days), it does sufficiently fix cells for subsequent analysis within that time period.

(Spec. 22: 17-29.)

FF3 In Example 1 of the Specification, "a volume of 50 µl of PNA [the sensor] is mixed into either a ThinPrep vial (Cytyc Corp.) or microfuge tube containing [a cell sample in] a volume of PreservCyt® (Cytyc Corp.) [the preservative solution] and the hybridization event takes place in solution" (Spec. 25: 28 to 26: 1). Following hybridization, the cells are separated from the preservative/sensor solution to remove unbound sensor, suspended in wash buffer, transferred to a slide, and reviewed for a positive reaction (*id.* at 26: 2-7).

FF4 Lorincz discloses several universal collection media (UCMs), which "make[ ] it possible to conveniently collect and preserve cells and their contents for assessment . . . from a single small patient sample, using cytological assays, molecular assays, or both" (Lorincz, col. 4, ll. 24-28).

FF5 Lorincz describes several formulations suitable as UCMs, including PreserveCyt® (Cytyc Corporation), which contains buffered methanol, and a number of UCMs containing 20% ethanol. None of the formulations contains formamide (Lorincz, col. 10, ll. 1-50).

FF6 Lorincz teaches that the UCMs permit "solution-based direct analysis of biomolecules of interest" (Lorincz, col. 2, ll. 17-18), avoiding "problems encountered in non-solution-based methods such as in situ

hybridization or non-direct methods which require separation of the biomolecule of interest from other cellular components before analysis" (*id.* at col. 2, ll. 19-23), and "prior art methods [which] require several extra steps, such as a separate concentration step, which . . . may result in many of the molecular components of the cell being degraded" (*id.* at col. 8, ll. 3-6).

FF7 Lorincz's UCMs are preservative solutions within the meaning of the Specification and the claims (**FF2**, **FF4**, **FF5**).

FF8 Lorincz discloses "[an] assay for nucleic acids [which] follows in general principle the method for detecting HIV [sic, HPV] RNA by the Digene Hybrid Capture HIV [sic, HPV] Test, described in WO 93/10263"[3] (Lorincz, col. 10, ll. 55-57). Lorincz's description of the assay begins in the middle of the Digene Hybrid Capture Test (i.e., the lysis step):

> Briefly, following lysis, 50 µl of probe mix (containing DNA biotinylated probe) [the sensor] was added to each well. The plate was sealed and incubated . . . for hybridization to occur. After hybridization, samples were transferred to a streptavidin-coated microplate, and 25 µl of anti-hybrid antibody was added to each well . . . a chemiluminescent substrate was added to each well [and] . . . the plate was read . . .

(Lorincz, col. 10, l. 58 to col. 11, l. 1).

FF9 The Examiner finds that "[t]he steps prior to lysis are addressed in Example 1 of WO93/10263 [Challberg] as comprising collection of cervical specimens in a preservative solution, hydrolysis reagent is added and following this lysis step, an [150 µl] aliquot was removed and added to the probe mix containing the sensor" (Ans. 20-21) "without an intermediate

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[3] WO 93/10263 is the Challberg reference cited by the Examiner in the obviousness rejection of claim 29.

washing step" (*id.* at 21). "Therefore, the alcohol present in the original preservative solution is maintained in the aliquot and the hybridization reaction occurs in some 'amount of' alcohol . . . meeting the limitation of the method as claimed" (*id.*).

FF10 Appellants acknowledge the Examiner's finding (on page 18 of the Office Action dated October 13, 2006) that there is "'…no indication that the original preservative solution in which the sample was maintained . . . was no longer present in the sample following the hydrolysis step. Therefore . . . the contacting does take place in a composition comprising the preservative solution.'" (App. Br. 7.) Appellants "disagree with the Examiner" on this point (*id.*), but do not specifically point out any error in the Examiner's finding.

PRINCIPLES OF LAW

"To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently." *In re Schreiber*, 128 F.3d 1473, 1477 (Fed. Cir. 1997).

During examination, the PTO must interpret terms in a claim using "the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description contained in the applicant's specification." *In re Morris*, 127 F.3d 1048, 1054 (Fed. Cir. 1997).

Nevertheless, "courts must not 'import[ ] limitations from the specification into the claim.' . . . [I]t is improper to 'confin[e] the claims to th[e] embodiments' found in the specification . . . ." *In re Trans Texas*

Holdings Corp., 498 F.3d 1290, 1299 (Fed. Cir. 2007) (citations omitted, bracketed text in internal quotes in original).

ANALYSIS

The Examiner finds that Lorincz describes universal collection media "which comprise . . . alcoholic preservative solution[s]" (Ans. 4), and "a method for identifying a sensor which specifically binds to a desired target" (*id.* at 3). The Examiner finds that Lorincz's Examples 1 and 3-5, where probes and "samples were incubated and hybridized in UCM formulations" (*id.* at 4), comprise contacting a sample suspected of containing the target with the sensor "in a preservative solution comprising an amount of one or more water soluble alcohols effective to preserve such solution against at least one contaminant" (*id.*), and therefore meet all the limitations of claim 28.

Appellants dispute that "contacting a sample with a sensor in the presence of a preservative solution is the same as contacting a sample with a sensor in a preservative solution" (App. Br. 8 (emphasis added)). Appellants contend that "[t]he method taught in [Lorincz and] WO 93/10263 . . . clearly requires that '…after hydrolysis, a 150µl aliquot was removed from the sample tube and added to 50µl of a probe diluent containing Probe A, B, or C' (emphasis added [by Appellants]) . . . . Thus, in Lorincz *et al.*, the contacting of a target of interest with a detectable sensor does not take place in a preservative solution as specified by the current claims" (*id.* at 6). Appellants contend that "[a]ll Examples described in Lorincz *et al.* . . . require the manipulation of preserved cells outside of the original solution in which the cells are collected. Whether the manipulation takes place on a

slide or in a separate well of a microplate, the cells are no longer in the original collection solution and no further hybridizations, bindings or other experimental protocols takes place in that solution" (*id.* at 8).

Appellants' arguments are not persuasive. The evidence of record supports the Examiner's finding that Lorincz removes a 150 μL aliquot from a larger volume of UCM (i.e., the preservative solution) containing the lysed cell sample, mixes that aliquot with 50 μL of a solution containing the sensor, and the hybridization reaction proceeds in that mixture (**FF8**, **FF9**), and Appellants have not established or argued otherwise. The fact that the 150 μL aliquot might have been removed from a larger volume in the original sample collection vial does not change its composition – the 150 μL aliquot still contains the UCM (i.e., preservative solution) when it is combined with the sensor for hybridization. Appellants have not established, or even argued, that the sample is separated from the UCM before hybridization takes place (**FF10**).

To the extent Appellants contend that Lorincz does not anticipate the claimed invention because the contacting step must take place in the original collection vial, the claims neither recite nor require that the contacting take place in the original collection vial.

CONCLUSION(S) OF LAW

Appellants have not established that the Examiner erred in finding that Lorincz describes contacting a sample suspected of containing a target of interest with a detectable sensor, where the contacting takes place in a water-soluble alcohol-containing preservative solution. Accordingly, the rejection of claim 28 as anticipated by Lorincz is affirmed.

ISSUE: OBVIOUSNESS

There are eight separate obviousness rejections of remaining claims 1-23, 26, 27, 29, 36, and 37, as set forth above in the Statement of the Rejection, but each of the rejections is based on the teachings of Lorincz, relied on as in the anticipation rejection, together with the teachings of one or more secondary references.

The issue raised by each of the obviousness rejections is the same issue raised by the anticipation rejection: Have Appellants established that the Examiner erred in finding that Lorincz describes contacting a sample suspected of containing a target of interest with a detectable sensor, where contacting takes place in a water-soluble alcohol-containing preservative solution?

ANALYSIS

Appellants essentially reiterate their arguments with respect to Lorincz in response to each of the eight obviousness rejections. For example, in response to the rejection of claims 1-4, 8-12, 14-16, 18-19, 23, 26, and 27 as unpatentable over Lorincz and Shah, Appellants contend that Lorincz "does not teach or suggest contacting a sample with a sensor in an alcoholic preservative solution that does not contain formamide under conditions in which the sensor can bind to the target" (App. Br. 10). Appellants contend that "[t]his deficiency cannot be overcome by Shah" (*id.*), thus, "[t]he Examiner has not pointed with specificity to any teaching or suggestion in Lorincz *et al.* or Shah *et al.*, either alone or in combination that recites all the limitations of claim 1" (*id.*).

Similarly, in response to the rejection of claims 20-22 as unpatentable over Lorincz, Shah, and Challberg, Appellants contend that "[t]he Examiner has not pointed with specificity to any teaching or suggestion in Lorincz *et al.* or Shah *et al.*, either alone or in combination that recites all the limitations of claim 1" (*id.* at 11) and "[t]his deficiency cannot be overcome by Challberg" (*id.*).

Appellants make analogous arguments in response to the rejection of claims 5, 7, 29, and 36-37 over Lorincz, Shah, and Hyldig-Nielsen (*id.* at 12-13); the rejection of claim 6 over Lorincz, Shah, and Kumar (*id.* at 13-14); the rejection of claim 10 over Lorincz, Shah, and Bruchez, Jr. (*id.* at 14-15); the rejection of claim 13 over Lorincz, Shah, and Ylikoski (*id.* at 15-16), and the rejection of claim 17 over Lorincz, Shah, and Fukasawa (*id.* at 15-16).

Finally, in response to the rejection of claim 29 as unpatentable over Lorincz and Challberg, Appellants contend "[t]he Examiner has not pointed with specificity to any teaching or suggestion in Lorincz *et al.* that recites all the limitations of claim 28" (*id.* at 12) and "[t]his deficiency cannot be overcome by Challberg" (*id.*).

Appellants do not identify any error in the Examiner's reasoning with respect to Lorincz beyond the arguments already addressed, and those arguments are not persuasive for reasons discussed above.

CONCLUSIONS OF LAW

Appellants have not established that the Examiner erred in finding that Lorincz describes contacting a sample suspected of containing a target of

interest with a detectable sensor, where contacting takes place in a water-soluble alcohol-containing preservative solution.

SUMMARY

- The rejection of claim 28 under 35 U.S.C. § 102(e) as anticipated by Lorincz is affirmed.

- The rejection of claims 1-4, 8-12, 14-16, 18, 19, 23, 26, and 27 under 35 U.S.C. § 103(a) as unpatentable over Lorincz and Shah is affirmed.

- The rejection of claims 20-22 under 35 U.S.C. § 103(a) as unpatentable over Lorincz, Shah, and Challberg is affirmed.

- The rejection of claim 29 under 35 U.S.C. § 103(a) as unpatentable over Lorincz and Challberg is affirmed.

- The rejection of claims 5, 7, 29, 36, and 37 under 35 U.S.C. § 103(a) as unpatentable over Lorincz, Shah, and Hyldig-Nielsen is affirmed.

- The rejection of claim 6 under 35 U.S.C. § 103(a) as unpatentable over Lorincz, Shah, and Kumar is affirmed.

- The rejection of claim 10 under 35 U.S.C. § 103(a) as unpatentable over Lorincz, Shah, and Bruchez is affirmed.

- The rejection of claim 13 under 35 U.S.C. § 103(a) as unpatentable over Lorincz, Shah, and Ylikoski is affirmed.

- The rejection of claim 17 under 35 U.S.C. § 103(a) as unpatentable over Lorincz, Shah, and Fukasawa is affirmed.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv)(2006).

AFFIRMED

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CYTYC CORPORATION
DARRY PATTINSON, SR. IP PARALEGAL
250 CAMPUS DRIVE
MARLBOROUGH, MA 01752